

1. [Bis2A 05.0 Introduction Biological reactions and catalysts](#)
2. [Bis2A 05.1 Chemical Reactions](#)
3. [Bis2A 05.2 Enzymes](#)

Bis2A 05.0 Introduction Biological reactions and catalysts

class="introduction"

A hummingbird needs energy to maintain prolonged periods of flight. The bird obtains its energy from taking in food and transforming the nutrients into energy through a series of biochemical reactions. The flight muscles in birds are extremely efficient in energy production. (credit: modification of work by Cory Zanker)



Virtually every task performed by living organisms requires energy. Energy is needed to perform heavy labor and exercise, but humans also use a great deal of energy while thinking, and even during sleep. In fact, the living cells of every organism constantly use energy. Nutrients and other molecules are imported, metabolized (broken down) and possibly synthesized into new molecules, modified if needed, transported around the cell, and may be distributed to the entire organism. For example, the large proteins that make up muscles are actively built from smaller molecules. Complex carbohydrates are broken down into simple sugars that the cell uses for energy. Just as energy is required to both build and demolish a building, energy is required for both the synthesis and breakdown of molecules. Additionally, signaling molecules such as hormones and neurotransmitters are transported between cells. Pathogenic bacteria and viruses are ingested and broken down by cells. Cells must also export waste and toxins to stay healthy, and many cells must swim or move surrounding materials via the beating motion of cellular appendages like cilia and flagella.

The cellular processes listed above require a steady supply of energy. From where, and in what form, does this energy come? How do living cells obtain energy, and how do they use it? This chapter will discuss different forms of energy and the physical laws that govern energy transfer. This chapter will

also describe how cells use energy and replenish it, and how chemical reactions in the cell are performed with great efficiency.

Bis2A 05.1 Chemical Reactions

By the end of this section, you will be able to:

- Distinguish between kinetic and potential energy, and between exergonic and endergonic chemical reactions
- Identify four forms of energy important in human functioning
- Describe the three basic types of chemical reactions
- Identify several factors influencing the rate of chemical reactions

One characteristic of a living organism is metabolism, which is the sum total of all of the chemical reactions that go on to maintain that organism's health and life. The bonding processes you have learned thus far are anabolic chemical reactions; that is, they form larger molecules from smaller molecules or atoms. But recall that metabolism can proceed in another direction: in catabolic chemical reactions, bonds between components of larger molecules break, releasing smaller molecules or atoms. Both types of reaction involve exchanges not only of matter, but of energy.

The Role of Energy in Chemical Reactions

Chemical reactions require a sufficient amount of energy to cause the matter to collide with enough precision and force that old chemical bonds can be broken and new ones formed. In general, **kinetic energy** is the form of energy powering any type of matter in motion. Imagine you are building a brick wall. The energy it takes to lift and place one brick atop another is kinetic energy—the energy matter possesses because of its motion. Once the wall is in place, it stores potential energy. **Potential energy** is the energy of position, or the energy matter possesses because of the positioning or structure of its components. If the brick wall collapses, the stored potential energy is released as kinetic energy as the bricks fall.

In the human body, potential energy is stored in the bonds between atoms and molecules. **Chemical energy** is the form of potential energy in which energy is stored in chemical bonds. When those bonds are formed, chemical energy is invested, and when they break, chemical energy is released. Notice that chemical energy, like all energy, is neither created nor

destroyed; rather, it is converted from one form to another. When you eat an energy bar before heading out the door for a hike, the honey, nuts, and other foods the bar contains are broken down and rearranged by your body into molecules that your muscle cells convert to kinetic energy.

Chemical reactions that release more energy than they absorb are characterized as exergonic. The catabolism of the foods in your energy bar is an example. Some of the chemical energy stored in the bar is absorbed into molecules your body uses for fuel, but some of it is released—for example, as heat. In contrast, chemical reactions that absorb more energy than they release are endergonic. These reactions require energy input, and the resulting molecule stores not only the chemical energy in the original components, but also the energy that fueled the reaction. Because energy is neither created nor destroyed, where does the energy needed for endergonic reactions come from? In many cases, it comes from exergonic reactions.

Forms of Energy Important in Human Functioning

You have already learned that chemical energy is absorbed, stored, and released by chemical bonds. In addition to chemical energy, mechanical, radiant, and electrical energy are important in human functioning.

- Mechanical energy, which is stored in physical systems such as machines, engines, or the human body, directly powers the movement of matter. When you lift a brick into place on a wall, your muscles provide the mechanical energy that moves the brick.
- Radiant energy is energy emitted and transmitted as waves rather than matter. These waves vary in length from long radio waves and microwaves to short gamma waves emitted from decaying atomic nuclei. The full spectrum of radiant energy is referred to as the electromagnetic spectrum. The body uses the ultraviolet energy of sunlight to convert a compound in skin cells to vitamin D, which is essential to human functioning. The human eye evolved to see the wavelengths that comprise the colors of the rainbow, from red to violet, so that range in the spectrum is called “visible light.”
- Electrical energy, supplied by electrolytes in cells and body fluids, contributes to the voltage changes that help transmit impulses in nerve

and muscle cells.

Characteristics of Chemical Reactions

All chemical reactions begin with a **reactant**, the general term for the one or more substances that enter into the reaction. Sodium and chloride ions, for example, are the reactants in the production of table salt. The one or more substances produced by a chemical reaction are called the **product**.

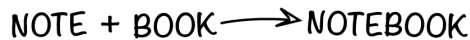
In chemical reactions, the components of the reactants—the elements involved and the number of atoms of each—are all present in the product(s). Similarly, there is nothing present in the products that are not present in the reactants. This is because chemical reactions are governed by the law of conservation of mass, which states that matter cannot be created or destroyed in a chemical reaction.

Just as you can express mathematical calculations in equations such as $2 + 7 = 9$, you can use chemical equations to show how reactants become products. As in math, chemical equations proceed from left to right, but instead of an equal sign, they employ an arrow or arrows indicating the direction in which the chemical reaction proceeds. For example, the chemical reaction in which one atom of nitrogen and three atoms of hydrogen produce ammonia would be written as $\text{N} + 3\text{H} \rightarrow \text{NH}_3$. Correspondingly, the breakdown of ammonia into its components would be written as $\text{NH}_3 \rightarrow \text{N} + 3\text{H}$.

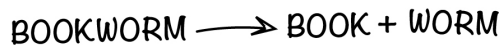
Notice that, in the first example, a nitrogen (N) atom and three hydrogen (H) atoms bond to form a compound. This anabolic reaction requires energy, which is then stored within the compound's bonds. Such reactions are referred to as synthesis reactions. A **synthesis reaction** is a chemical reaction that results in the synthesis (joining) of components that were formerly separate ([link](#)). Again, nitrogen and hydrogen are reactants in a synthesis reaction that yields ammonia as the product. The general equation for a synthesis reaction is $\text{A} + \text{B} \rightarrow \text{AB}$.

The Three Fundamental Chemical Reactions

a) In a synthesis reaction, two components bond to make a larger molecule. Energy is required and is stored in the bond:



b) In a decomposition reaction, bonds between components of a larger molecule are broken, resulting in smaller products:



c) In an exchange reaction, bonds are both formed and broken such that the components of the reactants are rearranged:



The atoms and molecules involved in the three fundamental chemical reactions can be imagined as words.

In the second example, ammonia is catabolized into its smaller components, and the potential energy that had been stored in its bonds is released. Such reactions are referred to as decomposition reactions. A **decomposition reaction** is a chemical reaction that breaks down or “de-composes” something larger into its constituent parts (see [\[link\]b](#)). The general equation for a decomposition reaction is: $AB \rightarrow A + B$.

An **exchange reaction** is a chemical reaction in which both synthesis and decomposition occur, chemical bonds are both formed and broken, and chemical energy is absorbed, stored, and released (see [\[link\]c](#)). The simplest form of an exchange reaction might be: $A + BC \rightarrow AB + C$. Notice that, to produce these products, B and C had to break apart in a decomposition reaction, whereas A and B had to bond in a synthesis reaction. A more complex exchange reaction might be: $AB + CD \rightarrow AC + BD$. Another example might be: $AB + CD \rightarrow AD + BC$.

In theory, any chemical reaction can proceed in either direction under the right conditions. Reactants may synthesize into a product that is later decomposed. Reversibility is also a quality of exchange reactions. For instance, $A + BC \rightarrow AB + C$ could then reverse to $AB + C \rightarrow A + BC$. This reversibility of a chemical reaction is indicated with a double arrow: $A + BC \rightleftharpoons AB + C$. Still, in the human body, many chemical reactions do

proceed in a predictable direction, either one way or the other. You can think of this more predictable path as the path of least resistance because, typically, the alternate direction requires more energy.

Factors Influencing the Rate of Chemical Reactions

If you pour vinegar into baking soda, the reaction is instantaneous; the concoction will bubble and fizz. But many chemical reactions take time. A variety of factors influence the rate of chemical reactions. This section, however, will consider only the most important in human functioning.

Properties of the Reactants

If chemical reactions are to occur quickly, the atoms in the reactants have to have easy access to one another. Thus, the greater the surface area of the reactants, the more readily they will interact. When you pop a cube of cheese into your mouth, you chew it before you swallow it. Among other things, chewing increases the surface area of the food so that digestive chemicals can more easily get at it. As a general rule, gases tend to react faster than liquids or solids, again because it takes energy to separate particles of a substance, and gases by definition already have space between their particles. Similarly, the larger the molecule, the greater the number of total bonds, so reactions involving smaller molecules, with fewer total bonds, would be expected to proceed faster.

In addition, recall that some elements are more reactive than others. Reactions that involve highly reactive elements like hydrogen proceed more quickly than reactions that involve less reactive elements. Reactions involving stable elements like helium are not likely to happen at all.

Video Link

So, how can you speed up chemical reaction? For an over view check out the following short (4 minute) video on chemical reactions by clicking [here](#).

Temperature

Nearly all chemical reactions occur at a faster rate at higher temperatures. Recall that kinetic energy is the energy of matter in motion. The kinetic energy of subatomic particles increases in response to increases in thermal energy. The higher the temperature, the faster the particles move, and the more likely they are to come in contact and react.

Concentration and Pressure

If just a few people are dancing at a club, they are unlikely to step on each other's toes. But as more and more people get up to dance—especially if the music is fast—collisions are likely to occur. It is the same with chemical reactions: the more particles present within a given space, the more likely those particles are to bump into one another. This means that chemists can speed up chemical reactions not only by increasing the **concentration** of particles—the number of particles in the space—but also by decreasing the volume of the space, which would correspondingly increase the pressure. If there were 100 dancers in that club, and the manager abruptly moved the party to a room half the size, the concentration of the dancers would double in the new space, and the likelihood of collisions would increase accordingly.

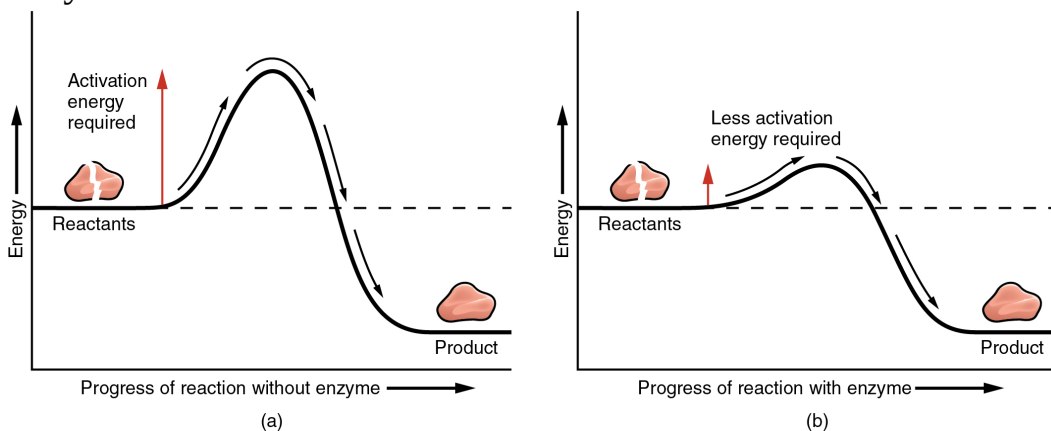
Enzymes and Other Catalysts

For two chemicals in nature to react with each other they first have to come into contact, and this occurs through random collisions. Because heat helps increase the kinetic energy of atoms, ions, and molecules, it promotes their collision. But in the body, extremely high heat—such as a very high fever—can damage body cells and be life-threatening. On the other hand, normal body temperature is not high enough to promote the chemical reactions that sustain life. That is where catalysts come in.

In chemistry, a **catalyst** is a substance that increases the rate of a chemical reaction without itself undergoing any change. You can think of a catalyst as a chemical change agent. They help increase the rate and force at which atoms, ions, and molecules collide, thereby increasing the probability that their valence shell electrons will interact.

The most important catalysts in the human body are enzymes. An **enzyme** is a catalyst composed of protein or ribonucleic acid (RNA), both of which will be discussed later in this chapter. Like all catalysts, enzymes work by lowering the level of energy that needs to be invested in a chemical reaction. A chemical reaction's **activation energy** is the “threshold” level of energy needed to break the bonds in the reactants. Once those bonds are broken, new arrangements can form. Without an enzyme to act as a catalyst, a much larger investment of energy is needed to ignite a chemical reaction ([link](#)).

Enzymes



Enzymes decrease the activation energy required for a given chemical reaction to occur. (a) Without an enzyme, the energy input needed for a reaction to begin is high. (b) With the help of an enzyme, less energy is needed for a reaction to begin.

Enzymes are critical to the body's healthy functioning. They assist, for example, with the breakdown of food and its conversion to energy. In fact, most of the chemical reactions in the body are facilitated by enzymes.

Summary

Chemical reactions, in which chemical bonds are broken and formed, require an initial investment of energy. Kinetic energy, the energy of matter in motion, fuels the collisions of atoms, ions, and molecules that are necessary if their old bonds are to break and new ones to form. All molecules store potential energy, which is released when their bonds are broken.

Four forms of energy essential to human functioning are: chemical energy, which is stored and released as chemical bonds are formed and broken; mechanical energy, which directly powers physical activity; radiant energy, emitted as waves such as in sunlight; and electrical energy, the power of moving electrons.

Chemical reactions begin with reactants and end with products. Synthesis reactions bond reactants together, a process that requires energy, whereas decomposition reactions break the bonds within a reactant and thereby release energy. In exchange reactions, bonds are both broken and formed, and energy is exchanged.

The rate at which chemical reactions occur is influenced by several properties of the reactants: temperature, concentration and pressure, and the presence or absence of a catalyst. An enzyme is a catalytic protein that speeds up chemical reactions in the human body.

Review Questions

Exercise:

Problem:

The energy stored in a foot of snow on a steep roof is _____.

- a. potential energy
- b. kinetic energy
- c. radiant energy
- d. activation energy

Solution:

A

Exercise:

Problem:

The bonding of calcium, phosphorus, and other elements produces mineral crystals that are found in bone. This is an example of a(n) _____ reaction.

- a. catabolic
- b. synthesis
- c. decomposition
- d. exchange

Solution:

B

Exercise:

Problem:

$AB \rightarrow A + B$ is a general notation for a(n) _____ reaction.

- a. anabolic
- b. endergonic
- c. decomposition
- d. exchange

Solution:

C

Exercise:

Problem:_____ reactions release energy.

- a. Catabolic
- b. Exergonic
- c. Decomposition
- d. Catabolic, exergonic, and decomposition

Solution:

D

Exercise:

Problem:

Which of the following combinations of atoms is *most likely* to result in a chemical reaction?

- a. hydrogen and hydrogen
- b. hydrogen and helium
- c. helium and helium
- d. neon and helium

Solution:

A

Exercise:

Problem:

Chewing a bite of bread mixes it with saliva and facilitates its chemical breakdown. This is *most likely* due to the fact that _____.

- a. the inside of the mouth maintains a very high temperature
- b. chewing stores potential energy
- c. chewing facilitates synthesis reactions

d. saliva contains enzymes

Solution:

D

Critical Thinking Questions

Exercise:

Problem:

$AB + CD \rightarrow AD + BE$ Is this a legitimate example of an exchange reaction? Why or why not?

Solution:

It is not. An exchange reaction might be $AB + CD \rightarrow AC + BD$ or $AB + CD \rightarrow AD + BC$. In all chemical reactions, including exchange reactions, the components of the reactants are identical to the components of the products. A component present among the reactants cannot disappear, nor can a component not present in the reactants suddenly appear in the products.

Exercise:

Problem:

When you do a load of laundry, why do you not just drop a bar of soap into the washing machine? In other words, why is laundry detergent sold as a liquid or powder?

Solution:

Recall that the greater the surface area of the reactants, the more quickly and easily they will interact. It takes energy to separate particles of a substance. Powder and liquid laundry detergents, with

relatively more surface area per unit, can quickly dissolve into their reactive components when added to the water.

Glossary

activation energy

amount of energy greater than the energy contained in the reactants, which must be overcome for a reaction to proceed

catalyst

substance that increases the rate of a chemical reaction without itself being changed in the process

chemical energy

form of energy that is absorbed as chemical bonds form, stored as they are maintained, and released as they are broken

concentration

number of particles within a given space

decomposition reaction

type of catabolic reaction in which one or more bonds within a larger molecule are broken, resulting in the release of smaller molecules or atoms

enzyme

protein or RNA that catalyzes chemical reactions

exchange reaction

type of chemical reaction in which bonds are both formed and broken, resulting in the transfer of components

kinetic energy

energy that matter possesses because of its motion

potential energy

stored energy matter possesses because of the positioning or structure of its components

product

one or more substances produced by a chemical reaction

reactant

one or more substances that enter into the reaction

synthesis reaction

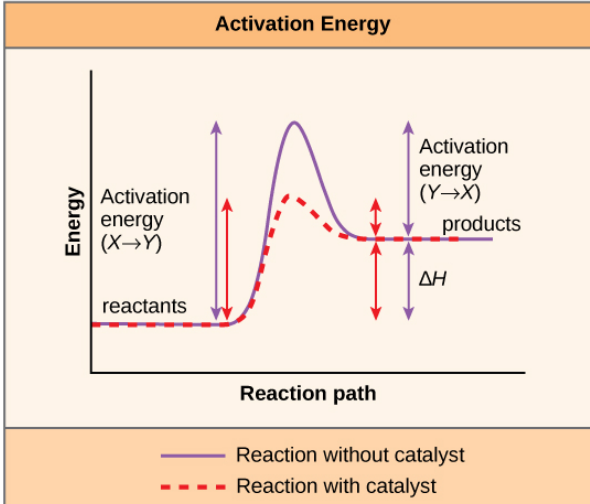
type of anabolic reaction in which two or more atoms or molecules bond, resulting in the formation of a larger molecule

Bis2A 05.2 Enzymes

By the end of this section, you will be able to:

- Describe the role of enzymes in metabolic pathways
- Explain how enzymes function as molecular catalysts
- Discuss enzyme regulation by various factors

A substance that helps a chemical reaction to occur is a **catalyst**, and the special molecules that catalyze biochemical reactions are called **enzymes**. Almost all enzymes are proteins, made up of chains of amino acids, and they perform the critical task of lowering the activation energies of chemical reactions inside the cell. Enzymes do this by binding to the reactant molecules, and holding them in such a way as to make the chemical bond-breaking and bond-forming processes take place more readily. It is important to remember that enzymes don't change the ΔG of a reaction. In other words, they don't change whether a reaction is exergonic (spontaneous) or endergonic. This is because they don't change the free energy of the reactants or products. They only reduce the activation energy required to reach the transition state ([\[link\]](#)).



Enzymes lower the activation energy of the reaction but do not change the free energy of the reaction.

Enzyme Active Site and Substrate Specificity

The chemical reactants to which an enzyme binds are the enzyme's **substrates**. There may be one or more substrates, depending on the particular chemical reaction. In some reactions, a single-reactant substrate is broken down into multiple products. In others, two substrates may come together to create one larger molecule. Two reactants might also enter a reaction, both become modified, and leave the reaction as two products. The location within the enzyme where the substrate binds is called the enzyme's **active site**. The active site is where the "action" happens, so to speak. Since enzymes are proteins, there is a unique combination of amino acid residues (also called side chains, or R groups) within the active site. Each residue is characterized by different properties. Residues can be large or small, weakly acidic or basic, hydrophilic or hydrophobic, positively or negatively charged, or neutral. The unique combination of amino acid residues, their positions, sequences, structures, and properties, creates a very specific chemical environment within the active site. This specific environment is suited to bind, albeit briefly, to a specific chemical substrate (or substrates). Due to this jigsaw puzzle-like match between an enzyme and its substrates (which adapts to find the best fit between the transition state and the active site), enzymes are known for their specificity. The "best fit" results from the shape and the amino acid functional group's attraction to the substrate. There is a specifically matched enzyme for each substrate and, thus, for each chemical reaction; however, there is flexibility as well.

The fact that active sites are so perfectly suited to provide specific environmental conditions also means that they are subject to influences by the local environment. It is true that increasing the environmental temperature generally increases reaction rates, enzyme-catalyzed or otherwise. However, increasing or decreasing the temperature outside of an optimal range can affect chemical bonds within the active site in such a way that they are less well suited to bind substrates. High temperatures will eventually cause enzymes, like other biological molecules, to **denature**, a process that changes the natural properties of a substance. Likewise, the pH of the local environment can also affect enzyme function. Active site amino acid residues have their own acidic or basic properties that are optimal for catalysis. These residues are sensitive to changes in pH that can impair the

way substrate molecules bind. Enzymes are suited to function best within a certain pH range, and, as with temperature, extreme pH values (acidic or basic) of the environment can cause enzymes to denature.

Induced Fit and Enzyme Function

For many years, scientists thought that enzyme-substrate binding took place in a simple “lock-and-key” fashion. This model asserted that the enzyme and substrate fit together perfectly in one instantaneous step. However, current research supports a more refined view called **induced fit** ([link](#)). The induced-fit model expands upon the lock-and-key model by describing a more dynamic interaction between enzyme and substrate. As the enzyme and substrate come together, their interaction causes a mild shift in the enzyme’s structure that confirms an ideal binding arrangement between the enzyme and the transition state of the substrate. This ideal binding maximizes the enzyme’s ability to catalyze its reaction.

Note:

Link to Learning



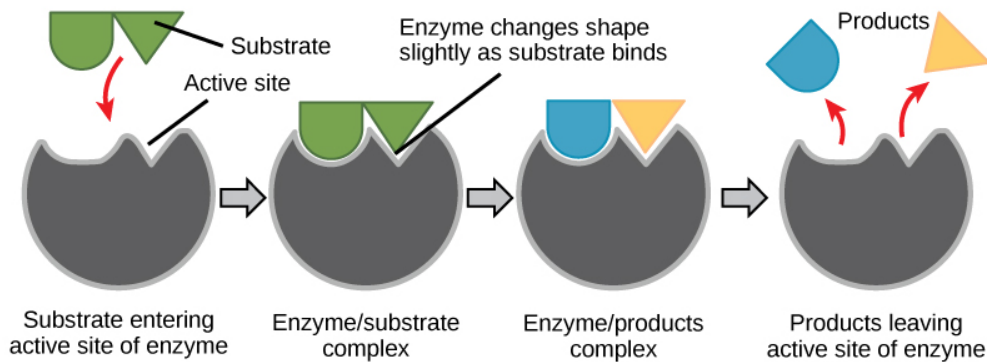
View an animation of induced fit at [this website](#).

Video Link

Here is another short video (2 minutes) from the University of Surrey on enzyme-substrate interactions. Click [here](#) for the video.

When an enzyme binds its substrate, an enzyme-substrate complex is formed. This complex lowers the activation energy of the reaction and promotes its rapid progression in one of many ways. On a basic level, enzymes promote chemical reactions that involve more than one substrate by bringing the substrates together in an optimal orientation. The appropriate region (atoms and bonds) of one molecule is juxtaposed to the appropriate region of the other molecule with which it must react. Another way in which enzymes promote the reaction of their substrates is by creating an optimal environment within the active site for the reaction to occur. Certain chemical reactions might proceed best in a slightly acidic or non-polar environment. The chemical properties that emerge from the particular arrangement of amino acid residues within an active site create the perfect environment for an enzyme's specific substrates to react.

You've learned that the activation energy required for many reactions includes the energy involved in manipulating or slightly contorting chemical bonds so that they can easily break and allow others to reform. Enzymatic action can aid this process. The enzyme-substrate complex can lower the activation energy by contorting substrate molecules in such a way as to facilitate bond-breaking, helping to reach the transition state. Finally, enzymes can also lower activation energies by taking part in the chemical reaction itself. The amino acid residues can provide certain ions or chemical groups that actually form covalent bonds with substrate molecules as a necessary step of the reaction process. In these cases, it is important to remember that the enzyme will always return to its original state at the completion of the reaction. One of the hallmark properties of enzymes is that they remain ultimately unchanged by the reactions they catalyze. After an enzyme is done catalyzing a reaction, it releases its product(s).



According to the induced-fit model, both enzyme and substrate undergo dynamic conformational changes upon binding. The enzyme contorts the substrate into its transition state, thereby increasing the rate of the reaction.

Control of Metabolism Through Enzyme Regulation

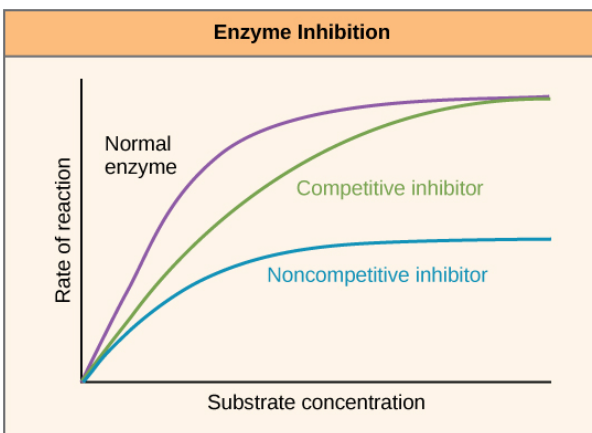
It would seem ideal to have a scenario in which all of the enzymes encoded in an organism's genome existed in abundant supply and functioned optimally under all cellular conditions, in all cells, at all times. In reality, this is far from the case. A variety of mechanisms ensure that this does not happen. Cellular needs and conditions vary from cell to cell, and change within individual cells over time. The required enzymes and energetic demands of stomach cells are different from those of fat storage cells, skin cells, blood cells, and nerve cells. Furthermore, a digestive cell works much harder to process and break down nutrients during the time that closely follows a meal compared with many hours after a meal. As these cellular demands and conditions vary, so do the amounts and functionality of different enzymes.

Since the rates of biochemical reactions are controlled by activation energy, and enzymes lower and determine activation energies for chemical reactions, the relative amounts and functioning of the variety of enzymes within a cell ultimately determine which reactions will proceed and at

which rates. This determination is tightly controlled. In certain cellular environments, enzyme activity is partly controlled by environmental factors, like pH and temperature. There are other mechanisms through which cells control the activity of enzymes and determine the rates at which various biochemical reactions will occur.

Regulation of Enzymes by Molecules

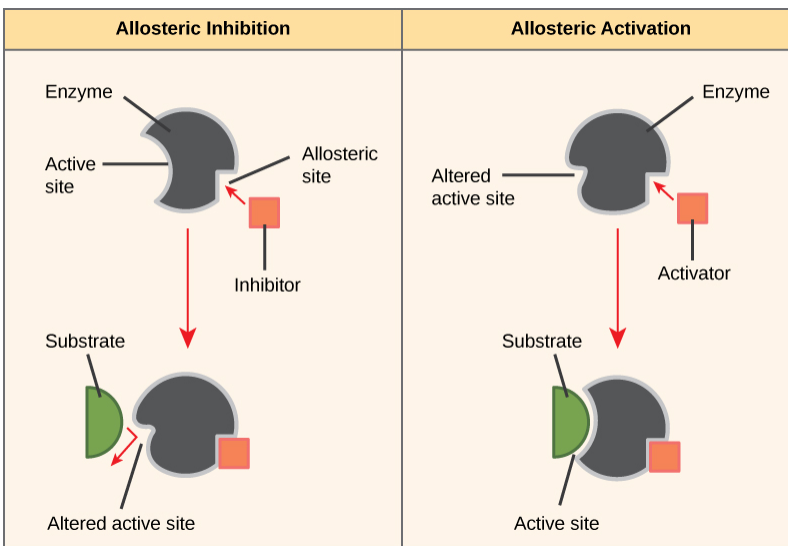
Enzymes can be regulated in ways that either promote or reduce their activity. There are many different kinds of molecules that inhibit or promote enzyme function, and various mechanisms exist for doing so. In some cases of enzyme inhibition, for example, an inhibitor molecule is similar enough to a substrate that it can bind to the active site and simply block the substrate from binding. When this happens, the enzyme is inhibited through **competitive inhibition**, because an inhibitor molecule competes with the substrate for active site binding ([link](#)). On the other hand, in noncompetitive inhibition, an inhibitor molecule binds to the enzyme in a location other than an allosteric site and still manages to block substrate binding to the active site.



Competitive and noncompetitive inhibition affect the rate of reaction differently. Competitive inhibitors affect

the initial rate but do not affect the maximal rate, whereas noncompetitive inhibitors affect the maximal rate.

Some inhibitor molecules bind to enzymes in a location where their binding induces a conformational change that reduces the affinity of the enzyme for its substrate. This type of inhibition is called **allosteric inhibition** ([\[link\]](#)). Most allosterically regulated enzymes are made up of more than one polypeptide, meaning that they have more than one protein subunit. When an allosteric inhibitor binds to an enzyme, all active sites on the protein subunits are changed slightly such that they bind their substrates with less efficiency. There are **allosteric activators** as well as inhibitors. Allosteric activators bind to locations on an enzyme away from the active site, inducing a conformational change that increases the affinity of the enzyme's active site(s) for its substrate(s).



Allosteric inhibitors modify the active site of the enzyme so that substrate binding is reduced or prevented. In contrast, allosteric activators modify the active site of the

enzyme so that the affinity for the substrate increases.

Video Link

Check out this short (1 minute) video on [competitive vs. noncompetitive](#) enzymatic inhibition. Also, take a look at this video (1.2 minutes) on [feed back inhibition](#).

Note:

Everyday Connection



Have you ever wondered how pharmaceutical drugs are developed? (credit: Deborah Austin)

Drug Discovery by Looking for Inhibitors of Key Enzymes in Specific Pathways

Enzymes are key components of metabolic pathways. Understanding how enzymes work and how they can be regulated is a key principle behind the development of many of the pharmaceutical drugs ([\[link\]](#)) on the market

today. Biologists working in this field collaborate with other scientists, usually chemists, to design drugs.

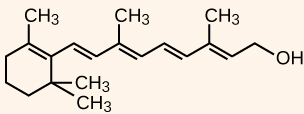
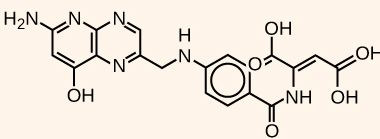
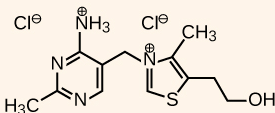
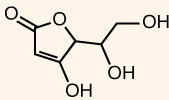
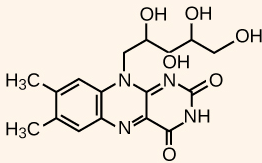
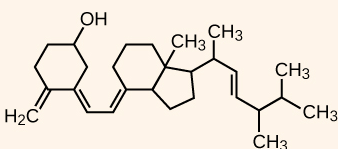
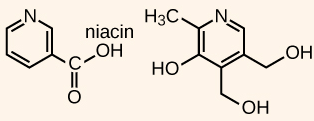
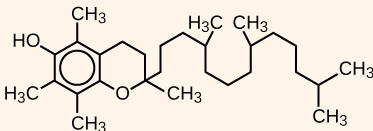
Consider statins for example—which is the name given to the class of drugs that reduces cholesterol levels. These compounds are essentially inhibitors of the enzyme HMG-CoA reductase. HMG-CoA reductase is the enzyme that synthesizes cholesterol from lipids in the body. By inhibiting this enzyme, the levels of cholesterol synthesized in the body can be reduced. Similarly, acetaminophen, popularly marketed under the brand name Tylenol, is an inhibitor of the enzyme cyclooxygenase. While it is effective in providing relief from fever and inflammation (pain), its mechanism of action is still not completely understood.

How are drugs developed? One of the first challenges in drug development is identifying the specific molecule that the drug is intended to target. In the case of statins, HMG-CoA reductase is the drug target. Drug targets are identified through painstaking research in the laboratory. Identifying the target alone is not sufficient; scientists also need to know how the target acts inside the cell and which reactions go awry in the case of disease.

Once the target and the pathway are identified, then the actual process of drug design begins. During this stage, chemists and biologists work together to design and synthesize molecules that can either block or activate a particular reaction. However, this is only the beginning: both if and when a drug prototype is successful in performing its function, then it must undergo many tests from in vitro experiments to clinical trials before it can get FDA approval to be on the market.

Many enzymes don't work optimally, or even at all, unless bound to other specific non-protein helper molecules, either temporarily through ionic or hydrogen bonds or permanently through stronger covalent bonds. Two types of helper molecules are **cofactors** and **coenzymes**. Binding to these molecules promotes optimal conformation and function for their respective enzymes. Cofactors are inorganic ions such as iron (Fe^{++}) and magnesium (Mg^{++}). One example of an enzyme that requires a metal ion as a cofactor is the enzyme that builds DNA molecules, DNA polymerase, which requires bound zinc ion (Zn^{++}) to function. Coenzymes are organic helper molecules, with a basic atomic structure made up of carbon and hydrogen,

which are required for enzyme action. The most common sources of coenzymes are dietary vitamins ([\[link\]](#)). Some vitamins are precursors to coenzymes and others act directly as coenzymes. Vitamin C is a coenzyme for multiple enzymes that take part in building the important connective tissue component, collagen. An important step in the breakdown of glucose to yield energy is catalysis by a multi-enzyme complex called pyruvate dehydrogenase. Pyruvate dehydrogenase is a complex of several enzymes that actually requires one cofactor (a magnesium ion) and five different organic coenzymes to catalyze its specific chemical reaction. Therefore, enzyme function is, in part, regulated by an abundance of various cofactors and coenzymes, which are supplied primarily by the diets of most organisms.

Dietary Vitamins	
Vitamin A 	Folic acid 
Vitamin B₁ 	Vitamin C 
Vitamin B₂ 	Vitamin D₂ (calciferol) 
Vitamin B₆ (pyridoxine) 	Vitamin E (alpha-tocopherol) 

Vitamins are important coenzymes or precursors of coenzymes, and are required for enzymes to function properly.

Multivitamin capsules usually contain mixtures of all the vitamins at different percentages.

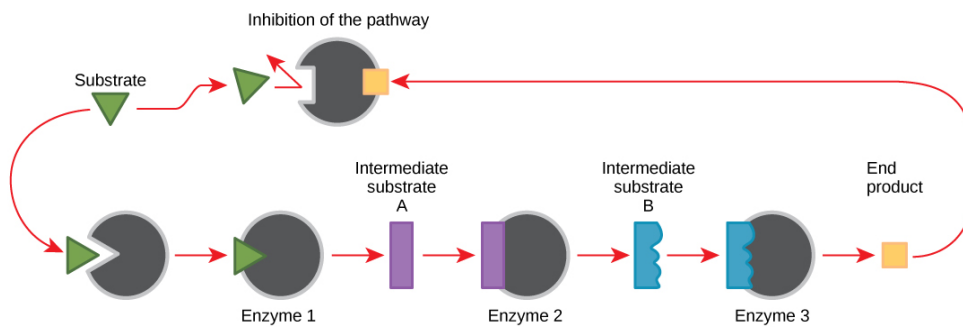
Enzyme Compartmentalization

In eukaryotic cells, molecules such as enzymes are usually compartmentalized into different organelles. This allows for yet another level of regulation of enzyme activity. Enzymes required only for certain cellular processes can be housed separately along with their substrates, allowing for more efficient chemical reactions. Examples of this sort of enzyme regulation based on location and proximity include the enzymes involved in the latter stages of cellular respiration, which take place exclusively in the mitochondria, and the enzymes involved in the digestion of cellular debris and foreign materials, located within lysosomes.

Feedback Inhibition in Metabolic Pathways

Molecules can regulate enzyme function in many ways. A major question remains, however: What are these molecules and where do they come from? Some are cofactors and coenzymes, ions, and organic molecules, as you've learned. What other molecules in the cell provide enzymatic regulation, such as allosteric modulation, and competitive and noncompetitive inhibition? The answer is that a wide variety of molecules can perform these roles. Some of these molecules include pharmaceutical and non-pharmaceutical drugs, toxins, and poisons from the environment. Perhaps the most relevant sources of enzyme regulatory molecules, with respect to cellular metabolism, are the products of the cellular metabolic reactions themselves. In a most efficient and elegant way, cells have evolved to use the products of their own reactions for feedback inhibition of enzyme activity. **Feedback inhibition** involves the use of a reaction product to regulate its own further production ([\[link\]](#)). The cell responds to

the abundance of specific products by slowing down production during anabolic or catabolic reactions. Such reaction products may inhibit the enzymes that catalyzed their production through the mechanisms described above.



Metabolic pathways are a series of reactions catalyzed by multiple enzymes. Feedback inhibition, where the end product of the pathway inhibits an upstream step, is an important regulatory mechanism in cells.

The production of both amino acids and nucleotides is controlled through feedback inhibition. Additionally, ATP is an allosteric regulator of some of the enzymes involved in the catabolic breakdown of sugar, the process that produces ATP. In this way, when ATP is abundant, the cell can prevent its further production. Remember that ATP is an unstable molecule that can spontaneously dissociate into ADP. If too much ATP were present in a cell, much of it would go to waste. On the other hand, ADP serves as a positive allosteric regulator (an allosteric activator) for some of the same enzymes that are inhibited by ATP. Thus, when relative levels of ADP are high compared to ATP, the cell is triggered to produce more ATP through the catabolism of sugar.

Additional Links

Khan Academy

The following links will take you to a series of videos on kinetics. The first link contains 4 videos on reaction rates and the second link contains 9 videos related to the relationship between reaction rates and concentration. These videos are supplemental and are provided to give you an outside resource to further explore enzyme kinetics.

- [Introduction to enzyme kinetics](#)
- [Reaction mechanism](#)

UCD Chemwiki

[Allosteric regulation](#)

Section Summary

Enzymes are chemical catalysts that accelerate chemical reactions at physiological temperatures by lowering their activation energy. Enzymes are usually proteins consisting of one or more polypeptide chains. Enzymes have an active site that provides a unique chemical environment, made up of certain amino acid R groups (residues). This unique environment is perfectly suited to convert particular chemical reactants for that enzyme, called substrates, into unstable intermediates called transition states. Enzymes and substrates are thought to bind with an induced fit, which means that enzymes undergo slight conformational adjustments upon substrate contact, leading to full, optimal binding. Enzymes bind to substrates and catalyze reactions in four different ways: bringing substrates together in an optimal orientation, compromising the bond structures of substrates so that bonds can be more easily broken, providing optimal environmental conditions for a reaction to occur, or participating directly in their chemical reaction by forming transient covalent bonds with the substrates.

Enzyme action must be regulated so that in a given cell at a given time, the desired reactions are being catalyzed and the undesired reactions are not. Enzymes are regulated by cellular conditions, such as temperature and pH. They are also regulated through their location within a cell, sometimes being compartmentalized so that they can only catalyze reactions under certain circumstances. Inhibition and activation of enzymes via other

molecules are other important ways that enzymes are regulated. Inhibitors can act competitively, noncompetitively, or allosterically; noncompetitive inhibitors are usually allosteric. Activators can also enhance the function of enzymes allosterically. The most common method by which cells regulate the enzymes in metabolic pathways is through feedback inhibition. During feedback inhibition, the products of a metabolic pathway serve as inhibitors (usually allosteric) of one or more of the enzymes (usually the first committed enzyme of the pathway) involved in the pathway that produces them.

Review Questions

Exercise:

Problem: Which of the following is not true about enzymes:

- a. They increase ΔG of reactions
- b. They are usually made of amino acids
- c. They lower the activation energy of chemical reactions
- d. Each one is specific to the particular substrate(s) to which it binds

Solution:

A

Exercise:

Problem: An allosteric inhibitor does which of the following?

- a. Binds to an enzyme away from the active site and changes the conformation of the active site, increasing its affinity for substrate binding
- b. Binds to the active site and blocks it from binding substrate
- c. Binds to an enzyme away from the active site and changes the conformation of the active site, decreasing its affinity for the substrate

d. Binds directly to the active site and mimics the substrate

Solution:

C

Exercise:

Problem:

Which of the following analogies best describe the induced-fit model of enzyme-substrate binding?

- a. A hug between two people
 - b. A key fitting into a lock
 - c. A square peg fitting through the square hole and a round peg fitting through the round hole of a children's toy
 - d. The fitting together of two jigsaw puzzle pieces.
-

Solution:

A

Free Response

Exercise:

Problem:

With regard to enzymes, why are vitamins necessary for good health? Give examples.

Solution:

Most vitamins and minerals act as coenzymes and cofactors for enzyme action. Many enzymes require the binding of certain cofactors or coenzymes to be able to catalyze their reactions. Since enzymes

catalyze many important reactions, it is critical to obtain sufficient vitamins and minerals from the diet and from supplements. Vitamin C (ascorbic acid) is a coenzyme necessary for the action of enzymes that build collagen, an important protein component of connective tissue throughout the body. Magnesium ion (Mg^{++}) is an important cofactor that is necessary for the enzyme pyruvate dehydrogenase to catalyze part of the pathway that breaks down sugar to produce energy. Vitamins cannot be produced in the human body and therefore must be obtained in the diet.

Exercise:**Problem:**

Explain in your own words how enzyme feedback inhibition benefits a cell.

Solution:

Feedback inhibition allows cells to control the amounts of metabolic products produced. If there is too much of a particular product relative to what the cell's needs, feedback inhibition effectively causes the cell to decrease production of that particular product. In general, this reduces the production of superfluous products and conserves energy, maximizing energy efficiency.

Glossary

active site

specific region of the enzyme to which the substrate binds

allosteric inhibition

inhibition by a binding event at a site different from the active site, which induces a conformational change and reduces the affinity of the enzyme for its substrate

coenzyme

small organic molecule, such as a vitamin or its derivative, which is required to enhance the activity of an enzyme

cofactor

inorganic ion, such as iron and magnesium ions, required for optimal regulation of enzyme activity

competitive inhibition

type of inhibition in which the inhibitor competes with the substrate molecule by binding to the active site of the enzyme

denature

process that changes the natural properties of a substance

feedback inhibition

effect of a product of a reaction sequence to decrease its further production by inhibiting the activity of the first enzyme in the pathway that produces it

induced fit

dynamic fit between the enzyme and its substrate, in which both components modify their structures to allow for ideal binding

substrate

molecule on which the enzyme acts